MORPHOLOGY

Lesions are frequently multiple and often involve deep gray matter as well as white matter and cortex. Periventricular spread is common. The tumors are relatively well defined in comparison with glial neoplasms but are not as discrete as metastases and often show extensive areas of central necrosis. Diffuse large-cell B-cell lymphomas are the most common histologic group. Within the tumor malignant cells infiltrate the parenchyma of the brain and accumulate around blood vessels. Reticulin stains demonstrate that the infiltrating cells are separated from one another by silver-staining material; this pattern, referred to as "hooping," is characteristic of primary brain lymphoma. The tumors express B cell markers such as CD20 and usually have a high growth fraction. When tumors arise in the setting of immunosuppression, various markers of Epstein-Barr virus are usually present in the tumor cells; the virus is usually detected by doing in situ hybridization for EBERs, small nuclear RNAs that are encoded by the viral genome.

Intravascular lymphoma, an unusual large cell lymphoma that grows within small vessels, often involves the brain along with other regions of the body. Instead of presenting as a mass lesion, the occlusion of vessels by malignant cells can result in widespread microscopic infarcts. Affected individuals often present with nonlocalizing neurologic symptoms, with the differential diagnosis usually including processes such as vasculitis or even dementia.

Germ Cell Tumors

Primary brain germ cell tumors occur along the midline, most commonly in the pineal and the suprasellar regions. They account for 0.2% to 1% of brain tumors in people of European descent but up to 10% in Japan. They are tumors of the young, with 90% occurring during the first two decades. Germ cell tumors, particularly teratomas, are among the more common congenital tumors. Germ cell tumors in the pineal region show a strong male predominance; this gender difference is not seen for suprasellar lesions.

The source of germ cells in the CNS is not clear; they may be "rests" that remain in the CNS or perhaps migrate there from other sites late in development. Germ cell tumors share many features with their counterparts in the gonads and mediastinum. In contrast to lymphomas, however, metastasis of a gonadal germ cell tumor to the CNS is common; thus, the presence of a non-CNS primary tumor must be excluded before a diagnosis of primary germ cell tumor of the CNS is made. The histologic classification of brain germ cell tumors is similar to that used in the testis (Chapter 21), but the tumor that is histologically similar to the seminoma in the testis is referred to as *germinoma* in the CNS. The responses to radiation therapy and chemotherapy parallel those of germ cell tumors arising at other sites. As in the periphery, CSF levels of tumor markers including α-fetoprotein and β-human chorionic gonadotropin may be useful for assisting diagnosis and tracking response to therapy.

Pineal Parenchymal Tumors

These lesions arise from specialized cells of the pineal gland (pineocytes) that have features of neuronal differentiation. The tumors range from well-differentiated lesions (*pineocytomas*), with areas of neuropil, cells with small, round nuclei, and no evidence of mitoses or necrosis, to high-grade tumors (*pineoblastomas*), with little evidence of neuronal differentiation, densely packed small cells with necrosis, and frequent mitotic figures. An intermediate form between these two extremes is also recognized. High-grade pineal tumors tend to affect children, while lower-grade lesions are found more often in adults. The highly aggressive pineoblastoma commonly spreads throughout the CSF space. It occurs with increased frequency in individuals with germ line mutations in *RB*. Gliomas are also found in the pineal region, arising from the glial stroma of the gland. Often low grade, these gliomas may extend into the posterior third ventricle.

Meningiomas

Meningiomas are predominantly benign tumors of adults, usually attached to the dura, that arise from the meningothelial cells of the arachnoid. Meningiomas may be found along any of the external surfaces of the brain as well as within the ventricular system, where they arise from the stromal arachnoid cells of the choroid plexus. Prior radiation therapy to the head and neck, typically decades earlier, is a risk factor for development of meningiomas. Other tumors such as metastases, solitary fibrous tumors, and a range of poorly differentiated sarcomas may also grow as dural-based masses.

Molecular Genetics. The most common cytogenetic abnormality is loss of chromosome 22, especially the long arm (22q). The deletions include the region of 22q12 that harbors the *NF2* gene, which encodes the protein merlin; as expected, meningiomas are a common lesion in the setting of NF2 (see later). Of sporadic meningiomas, 50% to 60% harbor mutations in the *NF2* gene; most of these mutations are predicted to result in absence of functional merlin protein. In meningiomas without *NF2* mutations, the most common mutations occur in TNF-receptor associated factor 7 (TRAF7), and identify a separate molecular subset of meningiomas with a tendency toward lower histologic grade and greater chromosomal stability. By contrast, higher grade meningiomas are more often associated with *NF2* mutations, loss of chromosome 22, and evidence of chromosomal instability (e.g., the presence of additional chromosomal aberrations).

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Meningiomas are usually rounded masses with well-defined dural bases that compress underlying brain but are easily separated from it (Fig. 28-53A). Extension into the overlying bone may be present. The surface of the mass is usually encapsulated by thin, fibrous tissue and may have a bosselated or polypoid appearance. They may also grow **en plaque**, in which the tumor spreads in a sheetlike fashion along the surface of the dura. This form is commonly associated with hyperostotic reactive changes in the adjacent bone. The lesions range from firm and fibrous to finely gritty, or they may contain numerous calcified psammoma bodies. Grossly evident necrosis and extensive hemorrhage are absent.